REMARKS

In view of the following Remarks, the Examiner is requested to withdraw the rejection and allow Claims 1-16 and newly presented Claims 81-83, the only claims pending and currently under examination in this application.

FORMAL MATTERS:

Claims 1, 3, 8, and 16 are amended. Support for these amendments may be found in the specification on page 11, lines 2 through 8 and on page 12, line 28 through page 13, line 9.

Claims 55-57 have been cancelled.

Claims 81-83 have been added. Support for Claim 81 may be found in the specification on page 12, line 28 through page 13, line 9. Support for Claim 82 and 83 may be found in the claims as originally filed.

No new matter is added. As such, the Examiner is requested to enter the above amendments.

OBJECTION TO THE CLAIMS

Claims 3, 8 and 16 have been objected to because they attempt to incorporate subject matter by reference to GenBank accession number "Hs.516830", which is considered non-patent literature that defines the limitations of the claims. The Applicants have amended the claims to remove the term "Hs.516830". In light of this amendment, withdrawal of the objection is requested.

REJECTIONS UNDER §112, ¶1

Claims 1-16 are rejected under 35 U.S.C 112, first paragraph, as failing to comply with the written description requirement.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 U.S.P.Q.2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991).

In making this rejection, the Examiner asserts that "these target proteins associated with cellular locomotion [Claim 1] and the genus of cyp4 proteins [Claim 3] comprises a number of proteins that have not been adequately defined or characterized. Both genus of proteins may include wild-type proteins, as well as naturally expressed variants. The written description in this instant case has not been adequately defined." (p. 4, l. 2-5) Further, the Examiner asserts that "There is no SEQ ID number set forth in the claims which corresponds to the listed proteins set forth in the claims, which would aid in clearly establishing what Applicants are in possession." (p. 4, l. 6-8) Finally, the Examiner asserts that "This claim language encompasses variants and mutants and polypeptides that share less than 100% sequence identity with the proteins. The specification does not evidence the possession of all the possible mutant polypeptides." (p. 5, l. 16-18)

The Applicants submit that the specification in view of the art provides suitable written description to support the element of Claim 1 of "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result." The specification teaches that target protein are proteins that may be associated with cellular locomotion, and a cellular locomotion protein is a protein that is involved or associated with cellular motility or movement from a first to a second location (p. 11, l. 24-26). The specification teaches that cellular locomotion proteins include those that are nucleus-associated ribbon-like structure proteins (p. 11, l. 24), and provides examples of four such proteins--LTB4DH, OKL38, C20orf139, and TRIM29 (p. 12, l. 6-21)--as well as members of the cyp4 family of proteins. The specification also teaches that cellular locomotion proteins include those that are those associated with the leading edge of a metastatic cell (p. 11, l. 32-34), and provides the example NTRK2/TrkB (p. 11, l. 34 – p. 12, l. 5). The specification describes all of these examples by GenBank accession numbers as well, which one of ordinary skill in the art would know how to search for in publicly available databases to identify the sequence represented by each gene name (p. 12, l. 1-21).

Furthermore, the art at the time of the invention was sufficiently well-developed that many more examples of cellular locomotion proteins were well-known; see, for example, the review by Ridley et al. (Science (2003) 302:1704-1709) (Exhibit A). Moreover, the level of skill in the art at the time of the invention was such that one of ordinary skill in the art could use publicly available databases to align potential target protein sequences with those of the claimed proteins to identify those that were substantially the same, which, as taught by the

specification, means that they share a sequence similarity of at least about 75%, including at least about 80, 85, 90, 95, 99% or higher, including 100% identity (p. 13, l. 19-22), and hence encompassed by the pending claims. Thus, one of ordinary skill in the art, reading the specification in view of the art, would conclude that the inventor was in possession of the invention comprising the claim element "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result."

Likewise, the Applicants submit that the specification in view of the art also provides suitable written description to support the genus of cyp4 proteins in Claim 3. The specification teaches that other proteins whose expression is similar to that of the cellular locomotion proteins are of interest (p. 12, l. 22-28), including the cyp4 family of proteins (p. 12, l. 29). The specification provides examples of five such proteins--cyp4F2, cyp4F3, cyp4F8, cyp4F11, cyp4F12 (p. 12, l. 29 – p. 13, l. 9)-and provides GenBank accession numbers such that one of ordinary skill in the art would be able to identify the sequence represented by each gene name (p. 12, l. 29 – p. 13, l. 9).

However, in the effort to expedite prosecution and without agreeing to the correctness of the rejection, Claim 3 has been amended to recite a cytochrome P450, family 4, subfamily f (cyp4F) protein. The USCS gene database (http://genome.ucsc.edu) teaches that the Cyp4F family of proteins comprises 7 known human proteins (cyp4F2, 3, 8, 11, 12 and 22) and a number of non-human homologs. The Applicants submit that the level of skill in the art at the time of the invention was such that one of ordinary skill in the art could use publicly available databases such as NCBI Blast to align potential target protein sequences with the sequences of cyp4 family proteins provided herein and in the UCSC gene database to identify other homologs that were substantially the same and hence encompassed by the pending claims. Accordingly, one of ordinary skill in the art, reading the specification in view of the art, would conclude that the inventor was in possession of the invention comprising the claim element "cyp4 proteins".

In view of the above amendments and remarks, reconsideration and withdrawal of the rejection is requested.

Claims 3, 9 and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

In making this rejection, the Examiner asserts that "Without sufficient guidance, the implementation of the claimed method utilizing sequences based on changeable accession numbers, which possibly represent different sequences, would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue." (p. 7, l. 1-4)

In view of the above amendments, it is believed that the rejection has been addressed and, as such, may be withdrawn.

REJECTIONS UNDER §112, ¶2

Claims 4 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The test for definiteness under 35 U.S.C. § 112, second paragraph, is whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576; 1 U.S.P.Q.2d 1081, 1088 (Fed. Cir. 1986).

In making this rejection, the Examiner asserts that "the recitation 'leading edge' in claims 4 and 5 is indefinite in that the term is allegedly superfluous and does not further clarify the claimed subject matter." (p. 7, l. 11-13)

Claim 4 recites "wherein said at least one target protein is a leading edge cellular locomotion protein." The Applicants submit that the specification teaches that "by leading edge cellular locomotion protein is meant that the protein, when present in a metastatic cell, localized to vesicles near or proximal to the leading edge of the cell membrane." (p. 11, l. 32-34). The art also teaches leading edges in migrating cells and proteins that are localized to leading edges. For example, Ridley et al. (Science (2003) 302:1704-1709) (Exhibit A) teaches the polarization of cells during migration and the localization of specific proteins to the leading and trailing edges of a polarized cell. Ridley et al. teaches the localization at the leading edge of proteins implicated in actin polymerization and adhesion formation, including PIP_3 (Fig. 1, panel A), phosphorylated α4-integrin (Fig. 1, panel B), CDC42, Rac, Profilin, ENA/VASP proteins,

ADP/Cofilin proteins, and actin capping proteins proteins (Fig. 2). Conversely, Ridley et al. teaches the localization at the rear of the cell of number of proteins implicated in actin depolymerization and adhesion disassembly, including FAK, Src, ERK, myosin II, microtubules, Rho, Calpain and Calcineurin (Fig. 2). Thus, the two domains are distinct cellular domains wherein distinct cellular events are occurring. Accordingly, the recitation of a cellular locomotion protein as a "leading edge" cellular locomotion protein as in pending Claim 4 does, in fact, provide a limitation upon the claim element. Reconsideration and withdrawal of the rejection is requested.

REJECTIONS UNDER §102

Claims 1, 2, 4-7 and 9-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25:439-446, 2001).

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, (Fed. Cir. 1987).

The standard for anticipation under section 102 is one of strict identity. An anticipation rejection requires a showing that each limitation of a claim be found in a single reference, *Atlas Powder Co. v. E.I. DuPont de Nemours & Co.,* 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). Further, an anticipatory reference must be enabling, see *Akzo N.V. v. United States Int'l Trade Comm'n* 808 F.2d 1471, 1479, 1 U.S.P.Q.2d 1241, 1245 (Fed. Cir. 1986), *cert denied*, 482 U.S. 909 (1987), so as to place one of ordinary skill in possession of the claimed invention. To anticipate a claim, a prior art reference must disclose every feature of the claimed invention, either explicitly or inherently. *Glaxo v. Novopharm, Ltd.* 334 U.S. P.Q.2d 1565 (Fed. Cir. 1995).

In making this rejection, the Examiner asserts that "Ricci discloses a method of assaying for the presence of neurotrophic tyrosine kinase receptor type 2 (NTRK2/TrkB), as well as other proteins associated with cellular locomotion in membranes from human bronchioalveolar carcinoma, adenocarcinoma, squamous cell carcinoma and small cell lung cancer using cytoplasmic immunostaining." (p. 8, l. 4-9)

The pending claims recite the claim elements of "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said

result to evaluate said cell's metastatic propensity." The specification teaches that a cellular locomotion protein is a protein that is involved or associated with cellular motility or movement from a first to a second location (p. 11, l. 25-26). The specification also teaches that in determining a cell's metastatic propensity, the subject invention provides methods of determining whether cells of a given tumor will spread from the tumor to other locations in a subject (p. 11, l. 2-8). Thus, the claimed method teaches assaying a cell for the presence of proteins associated with cellular motility and using the result of that assay to evaluate whether cells of a given tumor will spread from the tumor to other locations.

The Applicants submit that Ricci et al. does not anticipate the pending claims because Ricci et al. does not teach using the result of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential. Instead, Ricci et al. teaches correlation between cellular locomotion proteins and the growth and differentiation state of a malignancy. Ricci et al. teaches "NT and NT receptor expression was linked to tumor proliferative activity, using Ki-67 immunohistochemistry as a marker of tumor proliferation." (p. 439, col. 2, para. 3) Ricci et al. does not teach any correlation between NT and NT receptor expression and metastasis. Accordingly, Ricci et al. does not teach "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." Thus, Ricci et al. does not anticipate the pending claims. Reconsideration and withdrawal of the rejection is requested.

Claims 1-4, 6-11 and 13-16 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Application Publication number US 2002/0142981 A2.

In making this rejection, the Examiner asserts that "the publication discloses assaying markers for monitoring disease progression, such as the development of liver cancer. The nucleus associated ribbon-like structure proteins leukotriene B4 12-hydroxydehydrogenase (LTB4DH) and a cyp4 protein, cytochrome P450 were assayed." (p. 8, l. 11-15)

The pending claims recite the claim elements of "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." The specification teaches that cells can be assayed for the presence of one or more target proteins according to a variety of different

methods (p. 14, l. 11-12), and provides representative methods of protein detection (p. 14, l. 15 – p. 9).

The Applicants submit that US 2002/0142981 (hereafter the '981 publication) does not teach using the results of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential. Rather, the '981 publication teaches assaying for gene expression at the RNA level. The '981 publication teaches:

> [0033] The genes identified as being differentially expressed in liver cancer may be used in a variety of nucleic acid detection assays to detect or quantititate the expression level of a gene or multiple genes in a given sample. For example, traditional Northern blotting, nuclease protection, RT-PCR and differential display methods may be used for detecting gene expression levels. Those methods are useful for some embodiments of the invention. However, methods and assays of the invention are most efficiently designed with array or chip hybridization-based methods for detecting the expression of a large number of genes.

The Applicants submit that nowhere in the '981 publication does the publication teach assaying protein levels. Thus, the '981 publication does not teach "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity."

Furthermore, the Applicants submit that the '981 publication does not suggest the pending claims because it is well-understood in the art that RNA levels do not always correlate with protein levels. Accordingly, one of ordinary skill in the art would not be able to predict with any reasonable expectation of success that measurements of the protein levels of any of the genes disclosed in the '981 publication could be used to evaluate a cell's metastatic propensity, as taught by the pending claims.

Thus, the '981 publication does not teach or suggest the pending claims. Reconsideration and withdrawal of the rejection is therefore requested.

Claims 1-4 and 6-16 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number US 2006/0003391.

In making this rejection, the Examiner asserts that "the publication discloses methods of classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, such as cellular locomotion proteins tri-partite-containing motif 29 (TRIM29) and pregnancy-induced growth inhibitor (OKL38)." (p. 8, l. 18 – p. 9, l. 2).

As discussed above, the pending claims recite "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." Thus, the claimed method teaches assaying a cell for the presence of proteins associated with cellular motility and using the result of that assay to evaluate whether cells of a given tumor will spread from the tumor to other locations.

The Applicants submit that US 2006/0003391 (hereafter the '391 publication) does not anticipate the pending claims because the '391 publication does not teach using the result of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential. Rather, the '391 publication teaches reagents (antibodies) that can be used to classify particular classes of tumors, and using these classifications to correlate a tumor with therapeutic regimen or outcome, to identify appropriate therapies for particular classes or subclasses, and to predict outcomes based on class or subclass (p. 1, col. 2, para. 5). The particular classes of tumors that the '391 publication teaches the characterization of are subtypes of breast cancers (see Appendix C (para 301) and Appendix E (para 303)) and lung cancers (see Appendix D (para. 302) and Appendix F (para. 304)). The predictions that the '391 publication teaches are of the risk of recurrence of these cancers, described as the "Hazard Ratio", wherein the hazard ratio for each antibody reflects the predicted increase in risk of recurrence for each increase in the staining score, wherein scores greater than 1.0 in Appendices C-F indicate that staining predicts an increased risk of recurrence compared to an average individual (p. 19. col. 2, para. 241). However, nowhere in the '391 publication does the '391 publication teach predictions of metastatic potential. Thus, the '391 publication does not teach using the results of an assay to evaluate metastatic potential.

For example, the '391 publication teaches staining for TRIM29 and OKL38 in the context of classifying tumors as breast or lung cancer subtypes and using those classifications to predict recurrence of those cancer subtypes. For example, the '391 publications teaches that staining for TRIM29 (AGI IDs s0059 and s0059P2; see p. 29, entries 8 and 9) has a hazards ratio of greater than 1 for all three subtypes of breast cancer studied (Appendix C, l. 5) and thus is

predictive of an increased risk of recurrence of those cancer subtypes, whereas staining for OKL38 (AGI ID s0319; see p. 34, entry 6) is associated with lung cancers (p. 34, entry 6), with no association with particular lung cancer subtypes or any predictive power of risk of recurrence taught (no entries supplied in Appendices D or F). However, nowhere in the '391 publication does the '391 publication teach the use of TRIM29 or OKL38 staining to evaluate metastatic potential. Accordingly, the '391 publication does not teach "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." Thus, the '391 publication does not anticipate the pending claims. Reconsideration and withdrawal of the rejection is requested.

Claims 1-4 and 6-16 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application Publication number US 2006/0019256 A1.

In making this rejection, the Examiner asserts that "the publication discloses methods for characterizing and diagnosing lung cancer comprising assaying solid tumor cancer markers in samples of tissue from subjects. . . . The following cellular locomotion proteins were assayed TRIM29 (page 12, line 9), LTB4DH and C20orf139 (page 19)." (p. 9, l. 5-11)

As discussed above, the pending claims recite the claim elements of "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." Thus, the claimed method teaches assaying a cell for the presence of proteins associated with cellular motility and using the result of that assay to evaluate whether cells of a given tumor will spread from the tumor to other locations.

The Applicants submit that US 2006/0019256 A1 (hereafter the '256 publication) does not anticipate the pending claims because the '256 publication does not teach using the result of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential. Rather, the '256 publication teaches using a results of that assay to characterize a cell as a stem cancer cell.

Specifically, the '256 publication teaches that RNA levels of TRIM29 are elevated in unpassaged breast tumorigenic samples (UPTG) as compared to unpassaged non-tumorigenic samples (UPNTG) (Table 4, page 19), and that RNA levels of LTB4DH and C20orf139 are

elevated in unpassaged tumorigenic cells (UPTG) as compared to hematopoietic stem cells (HSC) (Table 5); see page 58, column 2, paragraph 338 for a description of the tables. The '256 publication teaches that genes with such profiles may be used as stem cell cancer markers (p. 58, col. 2, para 338). However, the Applicants submit that it is well known in the art that breast tumorigenic samples can be metastatic or non-metastatic, and the '256 publication does not provide a teaching of whether the samples used in their UPTG group were metastatic or non-metastatic (p. 58, col. 2, para. 338). Accordingly, one of ordinary skill in the art would not be able to predict if the genes listed in these tables were genes that could be used to evaluate metastatic potential with any expectation of success. Thus, the '256 publication does not teach the pending claim element of "using said result to evaluate said cell's metastatic propensity."

Furthermore, the Applicants submit that the '256 publication also does not teach the elements of the claim because, while the '256 publication attempts to assert that both nucleic acid sequences as well as the peptides encoded thereby may be used in the therapeutic and diagnostic methods and compositions of the method (p. 11, col. 2, para. 113), nowhere in the '256 publication does the '256 publication assay protein levels for any genes of the claimed genus. It is well understood in the art that RNA levels do not always correspond with protein levels. Accordingly, one of ordinary skill in the art would not be able to predict with any reasonable expectation of success that measurements of the protein levels of any cell locomotion genes disclosed in the '981 publication could be used as stem cell cancer markers, much less to evaluate a cell's metastatic propensity as taught by the pending claims. Thus, the '256 publication does not teach "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity."

Finally, the Applicants submit that the '256 publication also does not teach the elements of the claim because the '256 publication has not validated any of the genes taught in the claimed genus. These tables do not teach the extent of upregulation of the disclosed genes, the statistical significance of that reported upregulation, or any correlation of that upregulation with any function ascribed to stem cancer cells for any of the four single-spaced pages of genes for Table 4 (the table that calls out TRIM29) or six and a half single-spaced pages of genes for Table 5 (the table that calls out LTB4DH and C20orf139). Accordingly, the '256 publication does not teach "assaying said cell for the presence of at least one target protein associated with

cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity."

Thus, the '256 publication does not anticipate the pending claims. Reconsideration and withdrawal of the rejection is requested.

REJECTIONS UNDER §103(A)

Claims 1, 2, 4-7 and 9-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25:439-446, 2001) and further in view of U.S. patent Application Publication number US 2002/0142981 A1, U.S. Patent Application Publication number US 2006/0003391, and U.S. Patent Application Publication number US 2006/0019256 A1.

In order to meet its burden in establishing a rejection under 35 U.S.C. §103, the Office must first demonstrate that a prior art reference, or references when combined, teach or suggest all claim elements. *See, e.g., KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007); *Pharmastem Therapeutics v. Viacell et al.*, 491 F.3d 1342, 1360 (Fed. Cir. 2007); MPEP § 2143(A)(1). In addition to demonstrating that all elements were known in the prior art, the Office must also articulate a reason for combining the elements. See, *e.g., KSR* at 1741; *Omegaflex, Inc. v. Parker-Hannifin Corp.*, 243 Fed. Appx. 592, 595-596 (Fed. Cir. 2007) citing *KSR*. Further, the Supreme Court in *KSR* also stated that "a court *must* ask whether the improvement is more than the predictable use of prior art elements according to their established functions." *KSR* at 1740; emphasis added. As such, in addition to showing that all elements of a claim were known in the prior art and that one of skill had a reason to combine them, the Office must also provide evidence that the combination would be a predicted success.

In making this rejection, the Examine asserts that "Ricci et al. does not teach assaying nucleus-associated ribbon-like structure proteins, LTB4DH and a cyp4 protein, cytochrome P450. However, the publication '2981 teaches assaying markers LTB4DH and cytochrome P450 for monitoring disease progression such as the development of liver cancer." (p. 10, l. 4-9) Further, that "Publication '3391 teaches methods classifying tumors and assaying lung tumor sample for candidate tumor biomarkers, as well cellular locomotion proteins TRIM29, OKL38." (p. 10, l. 9-11) Finally, that "Publication '19256 teaches the following cellular locomotion proteins were assayed TRIM29, LTB4DH and C20orf139." (p. 10, l. 12-14)

The pending claims recite "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." The specification teaches that a cellular locomotion protein is a protein that is involved or associated with cellular motility or movement from a first to a second location (p. 11, l. 25-26). The specification also teaches that in determining a cell's metastatic propensity, the subject invention provides methods of determining whether cells of a given tumor will spread from the tumor to other locations in a subject (p. 11, l. 2-8). Thus, the claimed method teaches assaying a cell for the presence of proteins associated with cellular motility and using the result of that assay to evaluate whether cells of a given tumor will spread from the tumor to other locations.

As discussed above, the Applicants submit that Ricci et al. does not teach the pending claims because Ricci et al. does not teach using the results of an assay for proteins associated with cellular motility to evaluate metastatic potential. Rather, Ricci et al. teaches the correlation between cellular locomotion proteins and the growth and differentiation state of a malignancy (p. 439, col. 2, para. 3). Accordingly, Ricci et al. does not teach "assaying said cell for the presence of at least one target protein associated with cellular locomotion; and using said result to evaluate said cell's metastatic propensity."

Furthermore, Ricci et al. also does not suggest the elements of the pending claims because Ricci et al. with regard to assaying cellular locomotor proteins to evaluate a cell's metastatic propensity. Thus, Ricci et al. does not teach or suggest the claim elements "assaying said cell for the presence of at least one target protein associated with cellular locomotion; and using said result to evaluate said cell's metastatic propensity."

The Applicants submit that the '981, '391, and '256 publications do not remedy the deficiency because they, too, do not teach or suggest assaying for proteins associated with cellular locomotion and using that result to evaluate a cell's metastatic propensity. As discussed above, the '981 publication does not teach assaying protein levels, instead teaching measuring RNA levels (p. 3, col. 2, para. 33). The '391 publication does not teach using the results of an assay for proteins associated with cellular motility to evaluate metastatic potential, teaching instead to use such a result to evaluate risk of recurrence (See Appendices C-F and p. 19. col. 2, para. 241). The '256 publication does not teach using the results of an assay for proteins

associated with cellular motility to evaluate metastatic potential, teaching instead to use such a result to identify a stem cancer cell (p. 58, col. 2, para. 338). Accordingly, the '981, '391 and '256 publications do not teach or suggest the claim elements "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity" so as to remedy the deficiencies of Ricci et al.

Thus, Ricci et al. in view of US 2002/0142981 A1, US 2006/0003391, and US 2006/0019256 A1 does not render Claims 1, 2, 4-7 and 9-15 obvious. Reconsideration and withdrawal of the rejection is requested.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. patent Application Publication number US 2002/0142981 A1, and further in view of Ricci et al. (Am. J. Respir. Cell. Mol. Biol. 25:439-446, 2001) and further in view of U.S. Patent Application Publication number US 2006/0003391 and U.S. Patent Application Publication number US 2006/0019256 A1.

As discusses above, the pending claims recite "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity." Thus, the claimed method teaches assaying a cell for the presence of proteins associated with cellular motility and using the result of that assay to evaluate whether cells of a given tumor will spread from the tumor to other locations. The specification teaches that cells can be assayed for the presence of one or more target proteins according to a variety of different methods (p. 14, l. 11-12), and provides representative methods of protein detection (p. 14, l. 15 – p. 9).

As discussed above, the Applicants submit that the '981 publication does not teach the pending claims because the '981 publication does not teach using the results of an assay for the presence of a cellular locomotion protein to evaluate metastatic potential. Instead, the '981 publication teaches assaying for gene expression at the RNA level (p. 3, col. 2, para. 33). The Applicants submit that nowhere in the '981 publication does the publication teach assaying protein levels. Additionally, the '981 publication does not suggest assaying protein levels because it is well-understood in the art that RNA levels do not always correlate with protein levels. Accordingly, one of ordinary skill in the art would not be able to predict with any

reasonable expectation of success that measurements of the protein levels of any of the genes disclosed in the '981 publication could be used to evaluate a cell's metastatic propensity, as taught by the pending claims. Thus, the '981 publication does not teach or suggest the pending claim elements of "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity."

The Applicants submit that Ricci et al., the '391 publication and the '256 publication do not remedy the deficiency because they, too, do not teach or suggest assaying for proteins associated with cellular locomotion and using that result to evaluate a cell's metastatic propensity. As discussed above, Ricci et al. publication does not teach evaluating a cell's metastatic propensity, instead teaching a correlation between the cellular locomotion proteins and the growth and differentiation state of a malignancy (p. 439, col. 2, para. 3). The '391 publication does not teach using the results of an assay for proteins associated with cellular motility to evaluate metastatic potential, teaching instead to use such a result to evaluate risk of recurrence as defined by the Hazard Ratio in Appendices C-F (See Appendices C-f and p. 19. col. 2, para. 241). The '256 publication does not teach using the results of an assay for proteins associated with cellular motility to evaluate metastatic potential, teaching instead to use such a result to identify a stem cancer cell (p. 58, col. 2, para. 338). Accordingly, Ricci et al. and the '391 and '256 publications do not teach or suggest the claim elements of "assaying said cell for the presence of at least one target protein associated with cellular locomotion to obtain a result; and using said result to evaluate said cell's metastatic propensity" so as to remedy the deficiencies of the '981 publication.

Thus, US 2002/0142981 A1 in view of Ricci et al and further in view of US 2006/0003391 and US 2006/0019256 A1 does not render Claims 1-16 obvious. Reconsideration and withdrawal of the rejection is requested.

CONCLUSION

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number STAN-349.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: March 2, 2009

By: /Bret E. Field, Reg. No. 37,620/
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Enclosure(s): Exhibit A_Ridley.pdf

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